PHARMACEUTICAL COMPOSITION FOR COMPRESSED ANNULAR TABLET WITH MOLDED TRITURATE TABLET FOR BOTH INTRAORAL AND ORAL ADMINISTRATION

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a continuation of U.S. Ser. No. 10/015,930 filed Nov. 30, 2001 entitled "Pharmaceutical Composition for Compressed Annular Tablet with Molded Triturate Tablet for Both Intraoral and Oral Administration", by Jane C. Hirsh, Kamal K. Midha, Mark Hirsh, and Whe-Yong Lo.

FIELD OF THE INVENTION

This invention relates to a pharmaceutical composition that provides both for sublingual, buccal or vestibular mucosa or gingival application, hereafter referred to as intraoral administration and for chewed or sucked or swallowed hereafter referred to as oral administration. The pharmaceutical composition consists of two combined tablet portions, (1) a triturate tablet molded within the annulae of a second portion, and (2) a compressed tablet with a central cavity, hereafter referred to as a compressed annular tablet—CAT. The complete dosage form, hereafter referred to as compressed annular tablet with triturate tablet or CAT/T, comprises the triturate tablet molded into the compressed annular tablet through a manufacturing process. More particularly this invention relates to a triturate tablet composition containing at least one pharmaceutically active ingredient capable of intraoral administration and a compressed annular tablet with at least one pharmaceutically active ingredient capable of oral administration once the intraorally administered active ingredient has been substantially released. The invention further relates to a method of administering a pharmaceutical composition for both intraoral and oral administration to a patient. Furthermore, this invention combines two distinctly different pharmaceutical manufacturing processes to form one solid dosage unit: (1) employing dry powders or dried granulation to form a compressed annular tablet manufactured on a rotary tablet press, and (2) employing semi wet powders to form a molded triturate tablet manufactured on a tablet triturate machine.

BACKGROUND OF THE INVENTION

Intraoral administration of medicaments has been carried out according to the prior art. See U.S. Pat. No. 4,229,447 to PORTER. This patent discloses the intraoral administration of benzodiazepines including diazepam, lorazepam, oxazapam, temazapam, and chlordiazepoxide. According to Porter it is known in the art to administer benzodiazapines either orally or parenterally (i.e. by injection), especially intramuscularly or subcutaneously. Administering benzodiazepines by injection enables rapid attainment of effective plasma concentrations, that is more rapid than the plasma concentrations obtained following oral administration. One advantage of the intraoral administration as opposed to parenteral administration is that there is no injection site where pain and inflammation may develop. Another such advantage is that intraoral administration does not require sterilization of the preparations and the hypodermic syringes. Furthermore, in many situations self-administration of a medicament by parenteral means is not possible for a patient.

In U.S. Patent 5,739,136 to Ellinwood Jr. et al the medicament selected for intraoral administration is one that if given by oral administration is metabolized to an unwanted or aversive metabolite that is increasingly formed during gastrointestinal tract absorption and subsequent portal vein transport into the liver. Examples of such medicaments include not only the benzodiazepines especially a trifluorobenzodiazepine such as quazepam, but also other medicaments where it is advantageous to avoid first-pass metabolism such as the antianxiety/anticonvulsant/antihypnotic agents propoxyphene, nefazodone, trazodone, clomipramine, bupropion and combinations thereof. Unlike Porter, Ellinwood Jr. et al is not only concerned with rapidly attaining effective plasma concentrations of the intraorally administered medicament, but is especially concerned that the medicament include a drug where first pass-metabolism is to be avoided. The intraoral administration of the antianxiety/anticonvulsant/antihypnotic agents decreases the metabolism to the undesired metabolites.

In U.S. Pat. No. 6,183,778 to Jagotec A G, et al. the patent describes a multiple layer tablet capable of liberating one or more drugs at different release rates. This multi-layer dosage form is intended solely for oral administration and therefore must undergo first pass metabolism. Although it contains multiple releasing layers there is no dosage mechanism to provide the advantages presented by intraoral administration.

Remingtons, The Science and Practice of Pharmacy, 20th Ed., contains a complete history of dosage forms, including compressed tablets and triturate tablets; therefore, in the present invention no novelty is claimed in the broad practice of producing compressed tablets from dry powder or granulation or triturate tablets molded from a semi-wet powder. The uniqueness of the composition of this invention resides in its ability to provide in one dosage form the best features of both the compressed tablet and the triturate tablet.

The unique features of compressed tablets are well known in the art and is the dosage form most commonly employed as the method of choice for oral administration through which the tablets are digested and the drug absorbed into systemic circulation. Compressed tablets are not fragile and can withstand substantial handling without chipping or cracking. The compressed tablets can be formulated to provide disintegration and or dissolution of the active(s) at a specified time range after ingestion. They can be chewed but when used in this manner the tablets may lose some of their versatility. Compressed tablets can also be coated with a mixture containing a drug which will dissolve before the bulk of the tablet and may be absorbed intraorally. Compressed tablets may be layered, with one or more layers formulated to give early and rapid dissolution of drug in those layers as well as sustained dissolution of drugs in those layers. Compressed tablets may contain beads that are made of drugs in sustained-release or delayed-release forms in the tablet matrix.

Normally compressed tablets are uniformly solid but in this invention by employing tooling with a core rod, a ring shaped or annular tablet is produced, commonly referred to as a compressed annular tablet (CAT). Compressed tablets generally are intended to remain intact and not disintegrate until they reach the stomach or intestine. Compressed tablets are generally formulated with appropriate diluents or binders and/or polymers or waxes to obtain a desired appropriate hardness and are formulated as immediate, sustained or delayed released tablets.

Molded tablet triturates are, on the other hand, less versatile than compressed tablets. Tablet triturates usually